Effect of the Continuous Positive Airway Pressure on the Nocturnal Urine Volume or Night-time Frequency in Patients With Obstructive Sleep Apnea Syndrome

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OBJECTIVE To evaluate the effect of continuous positive airway pressure (CPAP) treatment on nocturnal urine volume, night-time urine frequency, and quality of life (QOL) in patients with obstructive sleep apnea syndrome (OSAS).

METHODS Ninety-eight participants with suspicious diagnosis of OSAS were prospectively enrolled in this study. Before polysomnography, measurement of the International Prostate Symptom Score—QOL score, the Overactive Bladder Symptom score (OABSS), the International Consultation on Incontinence Modular Questionnaire—Nocturia QOL were carried out to evaluate the lower urinary tract symptoms. During polysomnography, nocturnal urine volume and night-time urine frequency were recorded, and the concentrations of electrolytes in urine were determined. OSAS was confirmed in 92 patients, and 63 patients started to undergo CPAP treatment. Change in lower urinary tract symptoms—related QOL was assessed 1 month after CPAP treatment in 51 patients. Additionally, urine was collected at the time of CPAP titration in 25 patients.

RESULTS CPAP treatment significantly improved night-time frequency, which resulted in the improvement of total IPSS and QOL score. The night-time frequency questionnaire in OABSS similarly decreased, although total OABSS scores were not significantly improved. The International Consultation on Incontinence Modular Questionnaire—Nocturia QOL showed no significant changes after CPAP treatment. In addition to the night-time frequency, nocturnal urine volume and urine electrolyte contents significantly decreased after CPAP treatment.

CONCLUSION CPAP treatment decreases night-time urine frequency by reducing nocturnal urine volume and improves QOL in OSAS patients. UROLOGY 85: 333—336, 2015. © 2015 Elsevier Inc.

Nocturia is one of the most common urologic symptoms deteriorating quality of life (QOL) in many people.[1] Urinary tract infection; benign prostatic hypertrophy (BPH); overactive bladder; and malignant tumor of the bladder, prostate, and urethra may give rise to nocturia without polyuria. However, nocturia can also be caused by global or nocturnal polyuria as the early symptom of the systemic disease.[2]

Obstructive sleep apnea syndrome (OSAS) is a candidate cause of nocturnal polyuria. In patients with OSAS, the night-time frequency more than once at night is reported to increase by 52% up to 77%, depending on the severity of sleep-disordered breathing.[3,4]

A putative mechanism causing nocturnal polyuria in patients with OSAS is that the increasingly negative intrathoracic pressure caused by partial or full obstruction of the airway stimulates venous return to the right atrium, and atrial natriuretic peptide (ANP) secretion is increased in response to right atrium distension.[5-7]

Continuous positive airway pressure (CPAP) treatment, which keeps the respiratory tract patency by supplying air with positive pressure, is the one of the effective treatment for OSAS. Moreover, it has been reported that CPAP treatment improves not only the sleep-disorder breathing but also the urinary symptoms including night-time frequency.[8-12] However, the underlying mechanism by which CPAP treatment improves night-time frequency in OSAS patients has not yet been fully understood.

It is needed to uncover how much OSAS influences on voiding QOL and how much CPAP treatment contributes

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to the improvement of voiding QOL in OSAS patients. The present study has been designed to elucidate clinical features of patients with OSAS and investigate the impact of CPAP on nocturnal urine volume and voiding behavior in a prospective fashion.

METHODS

Study Design

This study was designed as a prospective study. The study protocol was conducted in accordance with the Declaration of Helsinki and the Ethical Guidelines for Clinical Research and approved by the institutional review boards in KKR Takamatsu Hospital (E40). All patients gave written informed consent before participating in the study.

Participants

Older than 20-year-old subjects undergoing polysomnography due to suspicious diagnosis of OSAS because of loud snoring, nocturnal choking, or daytime sleepiness were enrolled in this study between April and November 2012 at the Department of Sleep and Respiratory Center in KKR Takamatsu Hospital.

Subjects with active urinary tract infection, urolithiasis, interstitial cystitis, and uncontrollable complications were excluded from the study. Subjects who were treated with any form of α1-blocker, 5α-reductase inhibitor, or anticholinergic agent at least within 4 weeks before enrollment were excluded. Subjects who were treated with diuretics due to either congestive heart failure or renal failure were also excluded. In addition, subjects with hemoglobin A1c higher than the upper limit were excluded.

Study Protocol

All patients were screened by clinical interviews on their medical history and current medications. Their lower urinary tract symptoms (LUTS) including night-time frequency and QOL were evaluated using 3 questionnaires as follows: the International Prostate Symptom Score—QOL (IPSS-QOL) score, the Overactive Bladder Symptom Score (OABSS), and the International Consultation on Incontinence Modular Questionnaire—Nocturia QOL (ICIQ-Nqol). These questionnaires were translated into Japanese, and validity and reliability of Japanese version were confirmed.[13-15]

Nocturnal urine volume and night-time frequency were measured simultaneously with polysomnography. In this study, night-time frequency was defined as the total times of urination between going to bed to sleep and leaving the bed to get up. Nocturnal urine volume was measured during the time between going to bed and waking up in the morning. Therefore, it excludes the last void before going to bed but includes the first void after rising in the morning.[16]

Electrolytes (sodium, chloride, and potassium) in the nocturnal urine were determined. Biochemical profiles including hemoglobin A1c, serum blood urea nitrogen, and serum creatinine levels were examined to exclude subjects with uncontrolled diabetes mellitus and renal failure.

OSAS was diagnosed on the basis of full-night polysomnography in the sleep laboratory using a digital polysomnography system (Sleep Watcher E series; Teijin Pharma Limited, Tokyo, Japan). Apnea was defined as a complete airflow cessation for at least 10 seconds, and hypopnea was defined as a $\geq$50% reduction in airflow for at least 10 seconds followed by $\geq$3% oxygen desaturation. The apnea-hypopnea index (AHI) was calculated as the total number of apnea and hypopnea episodes per hour of sleep. The severity of OSAS was determined according to the American Academy of Sleep Medicine Task Force.[17]

Sixty-three patients were subjected to CPAP treatment. Most of them were the moderate to severe OSAS because the Japanese health insurance covers CPAP treatment for those with an AHI >20. After CPAP treatment at home for 1 month, patients underwent polysomnography under CPAP for titration. At the night of a CPAP titration, urinary specimens were taken again and follow-up questionnaires were recorded. For patients who did not undergo CPAP titration, only LUTS and QOL were assessed with the 3 instruments.

Table 1. Characteristics of the patients (n = 51) who underwent CPAP treatment for 1 month

Male:female	43:8
Age, y	55.9 ± 10.8
≥60 y, %	37.3
BMI, kg/m^2	26.8 ± 3.6
AHI, events/h	48.0 ± 25.9
Nadir SpO_2, %	75.6 ± 10.5

AHI, apnea-hypopnea index; BMI, body mass index; CPAP, continuous positive airway pressure; nadir SpO_2, nadir oxygen saturation during polysomnography.

Data are expressed as mean ± standard deviation.

Statistical Analyses

Data are presented as mean ± standard deviation. Changes of variables before and after CPAP treatment were evaluated using the Wilcoxon signed rank test. P values <.05 were considered statistically significant. Data analysis was performed with the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL), version 20, software for Windows.

RESULTS

Severity of OSAS and Adherence to CPAP Treatment

Ninety-eight subjects were enrolled into this study. Severity of OSAS was determined by polysomnography. Forty-four patients had severe OSAS (AHI >30), 26 had moderate OSAS (15< AHI <30), 21 had mild OSAS (5< AHI <15), and 6 did not experience OSAS (AHI <5). Consequently, 63 subjects (all the 44 patients with severe OSAS, 18 with moderate OSAS, and 1 with mild OSAS) were subjected to introduction of CPAP treatment. Nine patients dropped out by not being able to permit sleeping with CPAP treatment, and 3 patients were lost to follow-up. Finally, the effect of CPAP was analyzed in 51 subjects (43 men, 8 women; 38 patients with severe OSAS, 12 with moderate OSAS, and 1 with mild OSAS). Characteristics of the 51 subjects including age, body mass index, AHI, and nadir of SpO_2 are listed in Table 1. All the 51 patients had not been under medication for BPH-LUTS or overactive bladder at the time of CPAP treatment except for 3 patients. According to the adherence records in the Smart Card attached to the CPAP device, the mean rate of using CPAP was 75.3 ± 25.6% (range, 3.0%-100.0%), and the mean daily hours of using CPAP per night was 4.5 ± 1.6 hours (range, 1.1-7.1 hours).

Table 2. Change in the LUTS-related QOLs after CPAP treatment (n = 51)

Variable	Before CPAP Treatment (Mean ± SD)	After 1 mo of CPAP Treatment (Mean ± SD)	*P* Value
IPSS			
Total score	5.9 ± 4.7	4.8 ± 4.6	.031
Q1 (emptying)	0.7 ± 1.1	0.6 ± 0.8	.243
Q2 (daytime frequency)	1.6 ± 1.4	1.3 ± 1.3	.162
Q3 (intermittency)	0.4 ± 1.1	0.4 ± 1.0	.285
Q4 (urgency)	0.3 ± 0.6	0.3 ± 0.8	.805
Q5 (weak stream)	1.1 ± 1.6	0.9 ± 1.4	.115
Q6 (straining)	0.2 ± 0.4	0.3 ± 0.6	.317
Q7 (night-time frequency)	1.6 ± 1.3	1.1 ± 0.9	.003
QOL index	2.6 ± 1.4	2.1 ± 1.3	.003
OABSS			
Total score	2.5 ± 1.8	2.4 ± 1.7	.434
Q1 (daytime frequency)	0.5 ± 0.5	0.6 ± 0.5	.819
Q2 (night-time frequency)	1.3 ± 1.0	1.0 ± 0.8	.005
Q3 (urgency)	0.6 ± 0.9	0.7 ± 0.9	.310
Q4 (urge incontinence)	0.1 ± 0.4	0.1 ± 0.4	.480
ICIQ-Nqol			
Total score	87.1 ± 14.7	88.5 ± 13.6	.464
Q1-5,7 (sleep/energy)	84.1 ± 18.1	84.9 ± 17.0	.799
Q6,8-12 (bother/concern)	91.2 ± 13.2	93.0 ± 10.6	.493
Q13 (impact on QOL)	9.1 ± 1.5	9.0 ± 1.4	.597

ICIQ-Nqol, International Consultation on Incontinence Modular Questionnaire—Nocturia quality of life; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; OABSS, overactive bladder symptom score; QOL, quality of life; SD, standard deviation; other abbreviation as in Table 1.

Table 3. Change in polysomnographic and biochemical findings after CPAP treatment (n = 25)

Polysomnographic and Biochemical Profile	Before CPAP Treatment (Mean ± SD)	After 1 mo of CPAP Treatment (Mean ± SD)	*P* Value
AHI (events/h)	51.5 ± 28.7	3.4 ± 2.3	.000
Nadir SpO_2 (%)	76.4 ± 7.9	90.0 ± 4.1	.000
Night-time urine volume (mL)	542.4 ± 289.9	354.0 ± 217.4	.005
Night-time frequency (times)	2.0 ± 1.1	1.0 ± 1.2	.014
u-Na (mEq)	76.2 ± 36.2	51.5 ± 29.5	.004
u-Cl (mEq)	70.8 ± 40.2	48.2 ± 30.3	.007
u-K (mEq)	11.3 ± 5.3	9.0 ± 5.8	.025

u-Cl, urinary Cl contents; u-K, urinary K contents; u-Na, urinary Na contents; other abbreviations as in Tables 1 and 2.

Effect of CPAP Treatment on LUTS-related QOLs

Table 2 lists the effect of CPAP treatment for 1 month on LUTS-related QOL in the 51 subjects, most of whom had moderate or severe OSAS. The night-time frequency was significantly decreased after 1-month CPAP treatment, which resulted in significant improvement of total IPSS and QOL score. On the other hand, the remaining questionnaires of IPSS were not significantly changed after CPAP treatment. As to OABSS, the night-time frequency score was decreased, although this improvement did not result in an improvement of total OABSS. No beneficial effect of CPAP treatment was found on ICIQ-Nqol.

Effect of CPAP Treatment on Night-time Urine Volume or Frequency and Electrolytes

Among the 51 patients who underwent 1-month CPAP treatment, 25 patients underwent the CPAP titration again, whereas the remaining 26 patients did not undergo the CPAP titration due to personal reasons such as not having enough time for the titration or being reluctant to pay for the fee. The adherence to CPAP treatment in the 25 patients was not statistically different from that in the remaining 26 patients. Namely, the mean rate of using CPAP in the 25 patients was 74.9 ± 27.5% (range, 3.0%-100.0%), and the mean daily hours of using CPAP per night was 4.5 ± 1.4 hours (range, 1.5-6.4 hours), whereas the mean rate of using CPAP in the 26 patients was 75.6 ± 24.5% (range, 8.8%-100.0%), and mean daily hours of using CPAP per night was 4.5 ± 1.8 hours (range, 1.1-7.1 hours). The mean age of the 25 patients was 51.8 ± 9.9 years (range, 35-72 years), and the mean body mass index was 25.8 ± 2.6 kg/m^2 (range, 22.1-33.9 kg/m^2). Table 3 lists comparison of polysomnography and laboratory data in the 25 patients between the baseline and 1 month of CPAP treatment. AHI and nadir SpO_2 significantly improved after 1 month of CPAP treatment ($P = .000$ and .000, respectively). Both the nocturnal urine volume and the night-time frequency were significantly decreased after CPAP treatment ($P = .005$ and .014, respectively). Moreover, u-Na, u-Cl, and u-K were significantly decreased after CPAP treatment ($P = .004$, .007, and .025).

COMMENT

There have been several studies, which reported night-time frequency in patients with OSAS. Only few, however, have simultaneously investigated nocturnal urine frequency and volume together with QOL for subjects with suspicious diagnosis of OSAS. Moreover, few studied the impact of CPAP treatment on nocturnal urine frequency, volume, LUTS-related QOL, and urine electrolytes in patients with OSAS. The present study therefore is unique in that all the parameters previously mentioned have been comprehensively analyzed.

In the present study, most of the participants were relatively young and therefore might not have experienced clinically significant LUTS. Nevertheless, statistically significant improvement of total IPSS and QOL score were found after 1 month of CPAP treatment. These improvements could only be ascribed to the improvement of night-time urine frequency because there was no improvement as to the other 6 variables. The night-time frequency score (Q2) of OABSS also was improved after CPAP treatment, although there was no change in the questionnaire specialized for night-time frequency (ICIQ-Nqol). Such an improvement of the night-time urine frequency score is further supported by the reduction of night-time urine frequency in subjects who could afford to undergo second polysomnography after 1-month CPAP treatment. Reduction of night-time urine volume after 1-month CPAP treatment was remarkable, which is considered to be a major contributor to the reduction of night-time urine frequency. It was particularly interesting that reduction of night-time urine volume coincided with a decrease in nocturnal urine electrolytes.

One possible and reasonable explanation for the positive impact of CPAP treatment on nocturia is normalization of ANP secretion, although change in serum ANP after CPAP was not assessed in this study.

There are several limitations in the present study. Subjects with OABSS or LUTS due to BPH were not excluded completely, which might have made the relationship of OSAS with nocturnal urine frequency elusive. Nocturnal urine frequency and volume before and after CPAP treatment was respectively measured at only 1 night. Moreover, participants had to sleep under monitoring for polysomnography, which might have impaired the quality of sleep. These factors may affect QOL scores at night and nocturnal urine frequency.

CONCLUSION

CPAP treatment improves LUTS-related QOL in patients with OSAS through reduction of night-time urine frequency, which can be ascribed to the reduction of nocturnal urine volume and urinary electrolyte excretion at night.

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